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Cost Effectiveness
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RESEARCH

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The direct cost of chronic kidney disease (CKD) reported in Asian countries; a systematic literature review

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Abstract

Background The direct and indirect costs of chronic kidney disease (CKD) are substantial and increase over time. Concerns regarding our capacity to manage the financial burden that CKD) places on patients, caregivers, and society are raised by its increasing prevalence and progression. Lack of awareness of CKD's economic effects is a major reason that lawmakers and administrators pay little attention to this chronic illness.

Objective We aimed to analyze the direct burden of CKD across Asian countries and evaluate the main cost drivers among all mentioned cost centers in previous studies.

Methodology Related works evaluating the expenditures of CKD from the perspective of the patient were interpreted by a thorough search of PUBMED and GOOGLE SCHOLAR.

Results Country-wise, in Asia, the direct mean average medical costs in RRT patients were reported in 8 studies as $4574, $18668, $2901, $6848, $16669, $3489, $5945, and $6344 in Singapore, Korea, Taiwan, China, Jordan, Vietnam, Lebanon, and India respectively and the direct mean average medical costs in non-RRT patients were reported in six studies as $3412, $2241, $4534, $290 and $1500 in Singapore, Japan, China, Vietnam, and India respectively.

Conclusion Hemodialysis is the main cost driver having an average mean cost of $23,358 per patient per year while the average mean cost of disease management is $4977 per patient per year. More research is needed to understand the specific economic challenges disadvantaged populations face, including the impact of income, education, and access to healthcare resources on the financial burden of CKD.

Keywords CKD, ESRD, ESKD, Hemodialysis, Kidney disease management, Direct burden

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Introduction

Chronic kidney disease (CKD) is a progressive and irretrievable loss that is associated with significant morbidity and mortality. According to the 2015 Worldwide Burden of Disease Study, CKD ranked as the 12th major cause of mortality globally, resulting in approximately 1.1 million deaths [1]. CKD is also the 17th leading cause of disability-adjusted life years (DALYs) globally [2]. In 2017, approximately 35.8 million people experienced disability-adjusted life years all over. The prevalence of CKD is consequential, affecting nearly 850 million people worldwide, with a disproportionate burden falling on those with limited resources and other vulnerable populations. Notably, Asia, being the largest and most populous continent, bears a significant burden of kidney disease, with an estimated 450 million individuals affected in its eastern, southern, and south-eastern regions [3–5].

CKD is presented by the persistent loss of kidney function or a glomerular filtration rate (GFR) below 60 ml per minute per 1.73m^2 for three months or more. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines classify CKD based on GFR stages (G1–G5). Stage G1 is characterized by signs of kidney function loss but a preserved GFR > 90 ml per min; stage 2 involves mild kidney inefficiency with a GFR ranging from 60 to 90 ml per min; stage 3 is associated with moderate kidney function loss with a GFR of 30 to 59 ml per min; stage 4 signifies severe kidney function loss with a GFR of 15 to 29 ml per min; and stage 5 indicates a severe form of kidney failure also known as an end-stage renal disease (ESRD) with a GFR of 15 ml per min [6, 7].

CKD imposes a significant economic burden on a global scale due to the increased utilization of healthcare resources [8, 9]. Due to delayed diagnosis, most of the patients are at a chronic stage at the time of diagnosis. Chronic-stage patients are at increased risk of death, hospital admissions, and organ transplantation. This problem is frequent in underdeveloped countries in Asia and Africa [10]. The number of CKD patients receiving RRT (kidney replacement therapy) in Asia is expected to increase twofold, from 2.6 million in 2010 to 5.4 million by 2030 [11, 12].

Due to higher disability-adjusted life years, CKD is also associated with reduced productivity in affected patients. Unlike many chronic illnesses, where treatments have improved and allowed patients to live longer and more productive lives, many existing CKD and ESRD treatments (other than kidney transplants) do not significantly improve patient productivity [13–16]. The treatment of kidney failure varies greatly due to substantial geographic and ethnic diversity, which can be attributed to disparities in population density, socioeconomic factors, resource availability, the distribution of healthcare professionals, and healthcare policies [17]. Moreover, the establishment of chronic kidney disease (CKD) care programs in numerous countries has predominantly been influenced by payment processes, which in turn shape the delivery of care [18].

An aggregate forecast is inadequate and determining the components of treatment costs is critical for public decision-making; for example, analyzing the economic impact of changing care strategies, conducting cost-effectiveness studies, and developing a new treatment strategy. [15, 16, 19–22]. Most studies have focused on assessing the financial implications of CKD, primarily from the perspective of the well-being of physical fitness structure. Evidence on the monetary hardship of CKD is crucial for policymakers and healthcare administrators to make informed decisions regarding resource allocation, reimbursement policies, and healthcare financing. A systematic review can provide a robust evidence base for policy development and guide decision-making processes. We aimed to analyze the direct economic burden of CKD across Asian countries and evaluate the main cost drivers among all the cost centers mentioned in previous studies.

Methods

Study design

The systematic review adhered to the specifications delineated by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). To evaluate the economic burden of chronic kidney disease (CKD), this review incorporated studies that examined health resource utilization, the cost of illness, and the overall economic impact of kidney disease from the patient's perspective. Chronic kidney disease was divided into two main domains to segregate the direct cost of two different phases i.e. non-renal replacement therapy (NRRT) and renal replacement therapy (RRT). Non-renal replacement therapy phase; comprises stages like stage 1, stage 2, stage 3, and stage 4 of chronic kidney disease. At this phase of the disease, management cost includes all cost centers mentioned in previous studies that were specified as main cost centers like hospitalization costs, medication costs, lab investigations, physician visits, and other screening procedures while direct non-medical cost was reported as transportation cost. Another phase of the disease, i.e., stage 5 of CKD, also called ESRD, is named renal replacement therapy (RRT). The main cost drivers for RRT were reported as dialysis (hemodialysis and peritoneal dialysis) and kidney transplantation. Hemodialysis cost was calculated by aggregating the cost of all activities performed for that single hemodialysis session. Minor pre-dialysis surgical procedures like vascular access or fistula grafting costs were divided into average dialysis sessions. Peritoneal dialysis costs were calculated by sessions performed during one week and then converted to the annual cost. Transplantation cost was calculated as a monthly expense on maintenance and management aftercare and then aggregated as an annual cost. Total direct cost per year means all the costs of different cost centers of a particular phase in one year. The total annual direct cost of NRRT means all the medication costs, physician visits costs, lab investigations, diagnostic procedure performance costs, and transportation costs in one year. The total annual direct cost of RRT means dialysis procedure per session cost (pre-dialysis surgical procedure cost), transplantation procedure cost, medication related to dialysis and transplantation procedure, hospitalization, lab investigations, and physician visits costs in one year.

In a few studies, a broader perspective was adopted both from societal and patient perspectives. For such studies, patient perspective data of direct medical costs like expenditures directly affecting the patient, clearly reported in studies were extracted [23, 24]. The cost mentioned in the studies was converted to United States dollars with the same exchange rate as mentioned in the data collection years, then adjusted to the updated current inflation rates of July 2023 using the consumer price index (CPI) [15, 16]. All mentioned costs were converted to per patient per year cost to unify the data as shown in Table 2. Those studies in which overall cost was mentioned, were converted to per-patient cost by dividing total cost by sample size. Per-month and bi-annual costs were also converted to per-patient, per-year costs. The gross domestic product (GDP) for 2023 for each country was taken from the World Bank website.

Literature search

PUBMED, Cochrane, ScienceDirect, and Google Scholar databases were thoroughly searched until June 15, 2023 (the last date searched) for relevant papers analyzing the pharmacoeconomic evaluation of CKD from a patient perspective. The search strategy used for PUBMED involved specific search phrases and related tags to identify relevant articles. These search terms included 'chronic kidney disease [Mesh]', 'Economics/analysis [Mesh]', 'Cost of Illness [Mesh]', 'Health Care Economics and Organizations [Mesh]', 'burden [Mesh]', 'Health Care Costs [Mesh]', 'Costs and Cost Analysis [Mesh]', 'Costs and Chronic kidney disease [Mesh] '. Additionally, phrases such as 'cost of kidney disease', 'economic burden of ESRD', 'health care cost of dialysis', and 'economic evaluation of CKD' were used. The citation catalog of the included articles was also reviewed to identify any additional studies fulfilling the standards. The search was limited to original studies presented in English reporting the direct cost of CKD [24].

Inclusion and exclusion criteria

Two analysts separately reviewed the abstracts and titles, enlisting studies that met the following inclusion criteria: (i) well-defined CKD patients according to WHO-ICD (ICD-9, ICD-10) or KDIGO guidelines; (ii) the original study dealing with the cost of CKD patients through assets spent; (iii) to adapt and include the sub-analysis, outcomes from several studies should be measured using the same units or convertible units; and (iv) studies published after 2010. Editorials, narrative reviews, commentaries, posters at scientific conferences, meeting proceedings summaries, studies that only used model-based predictions and expert opinion to figure out costs, and studies that looked at the cost-effectiveness of certain drugs and interventions were not included in the analysis.

Quality assessment tool

The Allison Large Cost of Illness scale was used for quality assessment. A checklist of tools with relevant points was used; only cost-related parameters were used [44]. The 15-item quality evaluation test had a maximum score of 1 and a lowest score of 0, with each item being assessed. Studies with a total score of less than 10 were removed because they were of low quality. Three sections were used to classify that tool. The analytical framework was discussed in the first section. Which expenses ought to have been measured; comprised three questions about the study's purpose and viewpoint, the best epidemiologic strategy, and the specificity of the research question. The subject of the second segment was how well were resources used. Out of the five questions, one was omitted because it was deemed unnecessary (an intangible burden). Two questions about the study sample and two questions about the suitability of the evaluation period and the dependability of the data sources were also included. In the third portion; Eight elements, the first four concerning the analysis that addressed the study question, a range of estimates offered, the primary uncertainties discovered, and a sensitivity analysis. The final four concerns were sufficient documentation and explanation of cost components, data, sources, assumptions, and techniques, uncertainty around the estimates, significant restrictions addressed concerning cost components, data, assumptions and techniques, and outcomes.

Data extraction

We collected relevant data using modified abstraction sheets. The data extracted from the qualifying articles included information about the authors, the year of publication, the nation of the study, the purpose of the study, the design of the study, the data source, the study population, the perspective, the approach used, the methods of analysis, the results, and the method of diagnosing and classifying CKD (Table 1). The data extraction process was conducted independently, and the extracted data were carefully reviewed. The findings were then summarized in terms of direct costs and their various components, as shown in Table 2. These direct costs consisted of expenses related to medications, diagnostic services, outpatient consultations, emergency department visits, dialysis sessions, and inpatient hospitalizations.

Activity-Based Costing (ABC) is a method used to allocate costs to medical procedures, medications, or services by identifying different cost centers based on the activities involved in disease management. It aims to determine the actual cost by considering various resource-consuming activities. Conversely, "bottom-up costing" involves evaluating costs by aggregating individual components or activities. This method includes identifying all activities necessary for disease management, breaking down main activities into sub-cost activities that encompass all related costs, calculating the total overhead of each cost activity, and assigning the cost drivers (such as hours or units. For example, managing chronic kidney disease involves identifying cost centers like medication costs, pharmacy services, dialysis procedures, nursing staff services, physician visits, emergency visits, lab investigations, and various surgical procedures. In contrast, the "top-down" approach involves gathering cumulative data from the administration level and then segmenting different cost centers to determine the resources utilized for each patient individually.

Results

Screening results

There were 2150 possibly pertinent citations identified using the original literature search strategy. 1637 articles were filtered following titles and abstract scanning and the removal of 513 duplicates. For different reasons, 233 articles were eliminated even further. A final examination of 123 articles was conducted. This systematic analysis took into account 21 papers in total that satisfied the inclusion criteria according to the PRISMA diagram. Figure 1 shows the Study selection process, in line with the PRISMA guidelines [44].

Study characterization

Fourteen studies reported per-year cost per patient, five studies reported per-month cost per patient, and two studies reported per-six-month cost per patient. In fourteen studies, the CKD classification was according to KDIGO. Transportation costs are reported in five studies. Dialysis costs were reported in nine studies out of twenty-one studies from Asia. In ten studies, the reported method of data collection was prospective; in nine studies, cross-sectional; and in two studies, it was retrospective. characteristics of the included studies are

Table 1 Characteristics of the included studies

Country		Korea	Hong Kong	Palestine	China	Vietnam	India	Indonesia	Taiwan	Lebanon	Singapore	Iran	Jordan	Japan
Number of studies		1	1	1	4	1	4	1	1	2	2	1	1	1
Search	Electronic database search	1	1	1	4	1	3	1	1	1	2	1		1
	Hand search				1		1			1			1	
Currency	US$ (Dollars))	1	1	1	2	1	2	1	1	2	1			
	National currency				2		1				1		1	1
Data source	Retrospective, patient medical records	1		1	1	1		1					1	
	Retrospective, claims data		1		1		1			1	1			
	Prospective, patient medical records	1			2		2		1	1		1		1
	Retrospective and Prospective					1		1			1			
Cost reported	Direct cost		1	1	2		2		1		1	1		
	Economic burden	1			2		1	1		2	1		1	1
Costing method	Bottom-up approach	1			2	1	1			1			1	
	Top-down approach		1	1	2		2	1	1	1	1	1		1

Table 2 Summaries of studies included in the systematic review

Reference Country	Data year	Study design	Sample size	Diagnosis	Costing method	RRT costs	non-RRT costs
Younis et al., 2015 Palestine, [25]	2015	retrospective	N/A	N/A	Top-down approach	HD= $19,833 Pre-KT= $2340 KT-surgery= $7192 Post-KT= $4982	N/A
Al-shdaifat et al., 2013 Jordan, [13]	2010	Prospective	722	KDIGO	Bottom-up approach	Laboratory Test= $647 Medication Cost= $1023 Transportation cost=$832 AVF creation cost= $181 HD = $13,986	N/A
Kim et al. 2017, Korea [26]	2013	Prospective	1266	KDIGO	Bottom-up approach	Total direct cost=$ 18,668 HD=$49,996 PD= $43,005 KT= $109,403	N/A
Wong chen et al., 2019 Hong Kong [27]	2017	Prospective	402	N/A	Bottom-up approach	Dialysis HD= $52,307 PD= $27,529 nocturnal home HD= $28,097	N/A
Ma yu et al., 2020 China [28]	(2018–2020)	Prospective	111	KDIGO	ABC bottom-up approach	HD= $11,967	N/A
Nguyen et al., 2021 Vietnam [29]	2019	Cross-sectional	1175	N/A	Top-down approach	ESRD Direct cost stage5= $3489	CKD direct cost: Stage1= $27 Stage2= $36.11 Stage3= $81.28 Stage4= $1016
Josephine et al., 2022 India [30]	2018	Prospective	152	KDIGO	ABC bottom-up approach	HD= $ 6987	N/A
Afiatin et al., 2017 Indonesia [31]	2015	Cross-sectional	104	N/A	Top-down approach	Total direct cost PD=$ 3053 HD=$6249	N/A
Hong et al., 2023 China [32]	(2005–2019)	Prospective	508	KDIGO	ABC bottom-up approach	Total direct cost CAPD= $15,218 APD= $21,803 HD= $24,988 KT= $24,191	N/A
Esther et al., 2020 India [33]	2019	Cross-sectional	200	KDIGO	ABC bottom-up approach	Total direct cost= $6344 Medication cost=$581 HD= $5607	N/A
Wu et al., 2020 China [34]	2018	Cross-sectional	298	KDIGO	ABC bottom-up approach	HD= $14,297 PD= $13,419 KT= $25,665	N/A
Chang hwange et al., 2016 Taiwan [35]	(1998–2010)	Prospective	298	N/A	Top-down approach	Total direct cost HD = $23,479 PD = $19,300	N/A

Table 2 (continued)

Reference Country	Data year	Study design	Sample size	Diagnosis	Costing method	RRT costs	non-RRT costs
Aoun et al., 2022 Lebanon [12]	2019	Cross-sectional	160	KDIGO	ABC bottom-up approach	Total direct cost= $6195 Physician office visit = $129 Laboratory tests= $613 Medications= $342 Hospitalization= $ 1536 HD= $ 11,768 PD= $18,849	N/A
Rizk, et al., 2016 Lebanon [36]	2015	Retrospective	114	N/A	Bottom-up approach	Total direct cost= $5696 Medications=$315 Hospitalization= $1413 HD= $13,944 PD= $22,335	N/A
Al-Awsat Tiwari, et al., 2015 India [37]	2012	Cross-sectional	122	KDIGO	Bottom-up approach	Stage 5: Total direct cost $6344 HD= $3877	Stage 1–4: Direct cost = $1500
Low Lim, et al., 2019 Singapore [38]	2011–2015	Prospective	676	KDIGO	Bottom-up approach	N/A	Total direct cost for disease management, Stage1-2, $3661 Stage3, $4303 Stage4, $5776
Low Liu, et al., 2020 Singapore [39]	2011–2014	Prospective	1275	ICD-10	Bottom-up approach	N/A	Total direct cost, stage1 = $1240 Stage2= $2698 Stage3= $4076 Stage4= $5262
Abdi alinia, et al., 2022 Iran [40]	2021	Cross-sectional	266	ICD-9	Top-down approach	KT procedure cost = $1024 Note; (Willingness to pay for study)	N/A
Saito C, et al. 2019 Japan [41]	2012–2014	Prospective	70,627	KDIGO	Bottom-up approach	HD= $45,876	CKD Total mean cost, stage1= $2236 Stage2= $2161 Stage3= $2507 Stage4= $2963
Jian w, et al., 2017 China [42]	2013–2014	Retrospective	156	KDIGO	Top-down approach	HD =$23,849 PD =$19,027	CKD stage4; 1-yr Pre-HD cost= $ 4534 1-yr pre-PD cost= $7595
Ramachandran et al.,2013 India [43]	2011	Prospective	50	KDIGO	Top-down approach	KT (surgery cost) = $1943 KT (total expense) = $10,939	N/A

Notes Abbreviations PPY=per patient per year, HD=hemodialysis, PD=peritoneal dialysis, KT=transplantation; RRT costs=dialysis/transplantation dependent patients; non-RRT costs=non-dialysis dependent, non-ESRD

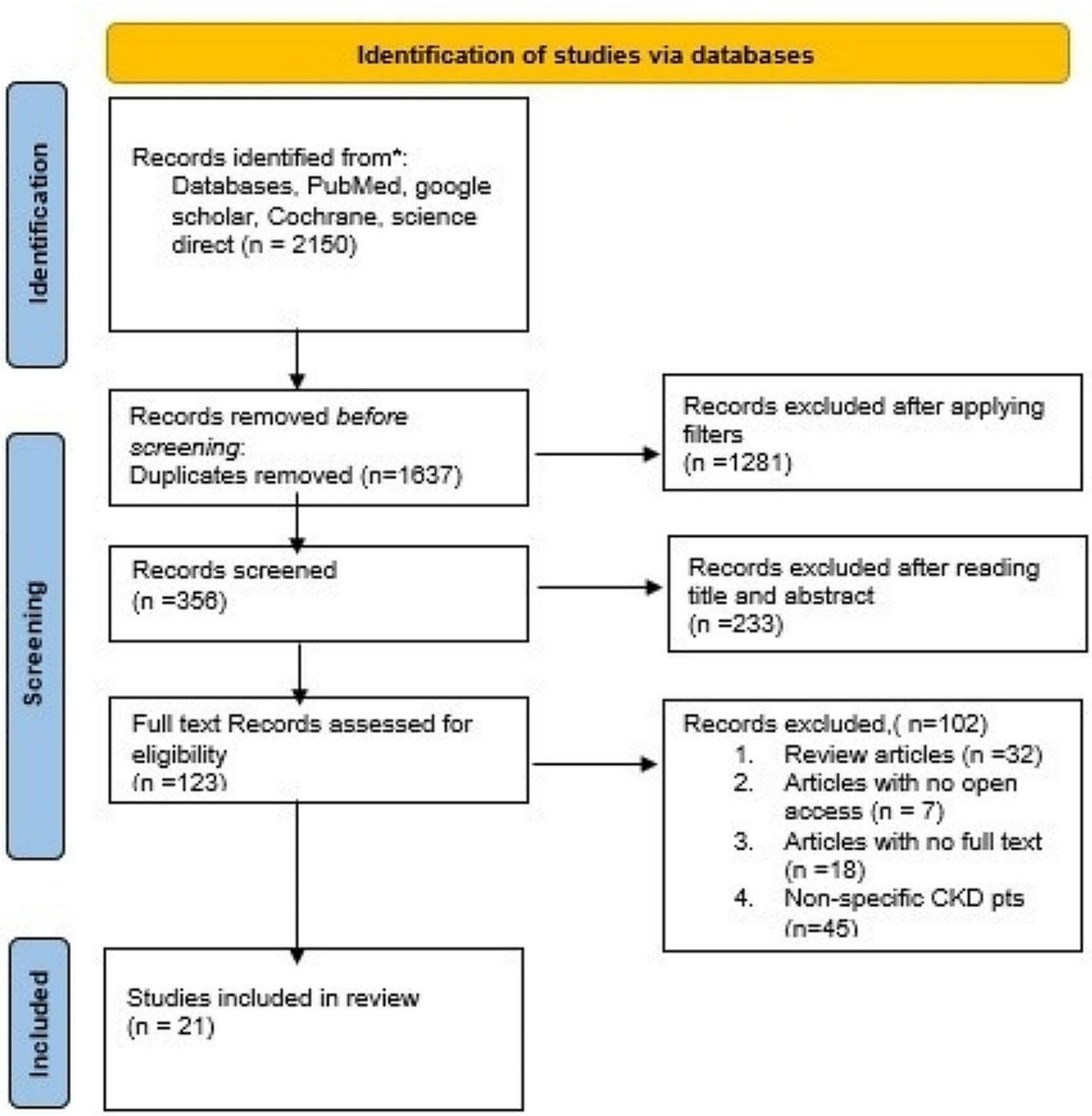

Fig. 1 PRISMA Flow diagram of a systematic review of the literature to select studies evaluating the direct burden of CKD in Asian countries

described in Table 2. Whereas, Summaries of included Studies in the Systematic Review are shown in data extraction Table 1.

The costing method in fifteen studies was an activity-based bottom-up approach, and in six studies, a top-down costing approach was used.

Direct cost results in Asia

RRT direct cost results

Country-wise, in Asia, the direct mean average medical costs in RRT patients were reported in 8 studies as $4574, $18,668, $2901, $6848, $16,669, $3489, $5945 and $6344 in Singapore, Korea, Taiwan, China, Jordan, Vietnam, Lebanon, and India respectively [12, 13, 26, 27, 29, 31, 35, 36]. The average mean direct cost is $4977. Direct costs were categorized as management costs, dialysis costs, and transplantation costs. A comparison of cost drivers of CKD in different Asian countries is shown in Fig. 2.

Non-RRT direct cost results

Country-wise, in Asia, the direct mean average medical costs in non-RRT patients were reported in six studies as $3412, $2241, $4534, $290, and $1500 in Singapore, Japan, China, Vietnam, and India respectively [12, 31, 35, 38, 39, 41]. The average mean direct cost is $1990 which is further categorized according to CKD stages.

Management cost

Hospitalization costs were reported in three studies from Asia. The average mean cost of hospitalization was

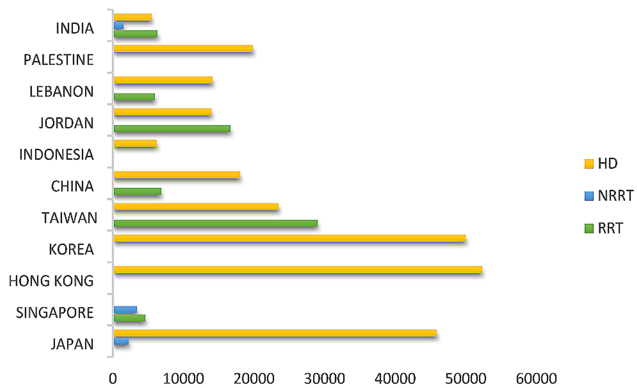

Fig. 2 Comparison of cost drivers of RRT and NRRT reported in different Asian countries

reported as $785. The average cost was higher as compared to India and China. Annual per-patient hospitalization costs in China, India, and Lebanon were reported as $ 404, $581, and $1331 respectively [12, 31, 35]. Hospitalization costs increased from $404 to $1331 as the disease progressed. The highest reported cost in Lebanon was $1331, and the lowest reported cost in China was $404. Patient medication costs were reported in four studies from Asia. The average cost was $1248. Medication costs were reported as $1023 in Jordan [13], $7.17 in Vietnam [29], and $328 in Lebanon [12]. The highest reported medication cost was $2175 from China, and the lowest reported medication cost was $7.17 from Vietnam [29]. Lab investigation costs were reported in three studies. The highest cost was reported from Lebanon [12] ($328) and the lowest from Vietnam ($7.17) [29]. The mean average cost of lab investigations was $420. Lebanon and Jordan reported that the cost was similar to the average mean cost. The annual physician visit cost reported in Vietnam was $6.15 and in Lebanon was $129. The average cost was $67. The AVF creation cost was reported only in Jordan at $181 [13]. Transportation costs were reported in five studies. The highest reported transport cost was $1711 from Korea [26], and the lowest reported transport cost was $24 from Vietnam [29]. The per-patient average mean annual cost of CKD management is shown in Table 3.

Dialysis cost

Hemodialysis costs were reported in sixteen out of twenty-one studies, and peritoneal dialysis costs were reported in six studies from Asia. The average mean direct cost of dialysis was $23,358. The highest cost of hemodialysis was mentioned as Hong Kong's $52,307 [27], India's $5490 [37], Lebanon's $14,117 [36], Jordan's $13,986 [13], Korea $64,145 [26], China $18,032 [34], and Taiwan $23,479 [35], ranging from a maximum from Hong Kong $52,307 [27]to a minimum of $14,117 from Lebanon [36]. The mean annual cost of hemodialysis and peritoneal dialysis among Asian countries is shown in Table 3. The mean average cost of peritoneal dialysis was $23,259. Maximum peritoneal dialysis cost was reported as $43,005 from Korea [26] and the minimum direct cost was reported as $3053 from Indonesia [31].

Transplantation cost

Transplantation costs are only reported in six studies. The highest transplantation cost from South Korea was $109,403 [26], reported as total direct medical cost, and the lowest cost reported from Iran was $1024 [40], this reported cost was only for the surgical procedure of transplantation. In two studies cost components of renal transplant were reported in detail like medicines, hospitalization, investigations, before and after referral, and other transplant expenditures like post-surgery cost and pre-surgery cost. In two other studies only overall annual post-surgery maintenance expenditures are mentioned, in three studies; only surgical procedure costs are mentioned.

Discussion

Due to the variations in the prices covered and the methodological variances after measuring and assessing costs, it is difficult to compare these countries with one another directly. We used GDP per capita to compare with the per-patient annual cost to evaluate direct economic burden [45, 46]. Gross Domestic Product (GDP) is a measure of the total economic output of a country. While it is not a direct indicator of affordability or disease management, it can provide some insights into a country's overall economic capacity and resources, which can indirectly influence its ability to manage diseases and provide healthcare services.

Per capita GDP is calculated by dividing the total GDP of a country by its population. It provides an average income level per person. Higher per capita GDP generally indicates a higher standard of living and potentially better access to healthcare resources. Countries with higher per capita GDP may have more resources to invest in healthcare infrastructure, research, and development of medical technologies.

The research topic focuses on the direct burden of CKD. CKD refers to the advanced stage of kidney disease, where the kidneys are unable to function adequately to sustain life. This condition requires long-term dialysis or kidney transplantation for survival. The direct burden of CKD refers to the financial costs associated with the disease, including medical expenses such as dialysis treatments, medications, surgeries, and hospitalizations. These costs can be substantial and place a significant financial strain on individuals, families, and healthcare systems. The mean direct cost is $4977. This average cost is almost similar, as reported in a study from Indonesia

Table 3 Annual per patient cost ($) of CKD (RRT&NRRT) treatment in Asian countries

Cost centers	Singapore (40, 41)	Japan (43)	Hong Kong (29)	Korea (28)	Taiwan (37)	China (30, 36)	Jordan (13)	Indonesia (33)	Iran (42)	Vietnam (31)	Lebanon (12, 38)	Palestine (27)	India (32, 35, 39, 43)
No of studies	2	1	1	1	1	4	1	1	1	1	2	1	4
GDP per capita USD (2023)	87,884	52,120	51,168	33,147	32,339	14,096	4851	4691	4234	4122	4003	1129	2650
Renal replacement therapy cost													
hemodialysis		45,876	52,307	64,145	23,479	18,032	13,986	6249			14,117	19,833	5490
Peritoneal dialysis			27,529	43,005	19,300	15,888		3053			22,613		
Transplantation surgery									1024			7192	1943
Transplantation total expense (pre + post-surgery)				109,403		24,928							10,939
AVF creation							181						
hospitalization		28,235				404					1372		581
medications						2175	1023			7.17	328		
lab investigations							647			51	564		
physician visits		366								6	129		
transportation				1711			832			24.77	48		273
Total direct cost of ESRD (RRT)	4574			18,668	29,013	6848	16,669			3489	5945		6344
Non-renal replacement therapy cost													
CKD stage 1	1240	2236								27			
CKD stage 2	2698	1261								36.11			
CKD stage 3	4189	2507								81.28			
CKD stage 4	5519	2963				4534				1016			
Total direct cost (NRRT)	3412	2241								290			1500

Per patient per year mean average cost reported in US dollars ($) *GDP; gross domestic product per capita

[31]. The direct burden is too high in Indonesia [31]. A very low burden is reported in Vietnam [29] and Hong Kong [27].

According to the findings of this review, CKD has a significant economic impact on the healthcare systems of Asian countries. Dialysis, hospitalization, medication use, physician visits, and lab investigations are substantial contributors to direct costs.

Singapore, with a GDP of $87,884, is among the most prosperous Asian countries. The direct cost of the disease reported is $4574. Both Studies evaluated cost from the patient's perspective. The results of both studies are in the same index of expenditures and resources utilized. Expenditures are within affordability.

Japan is among the upper-middle high-income countries in Asia, having a $52,133 GDP per capita [41]. Hospitalization cost and physician visit cost reported were $28,235. Based on "The Specific Health Check and Guidance in Japan," 105,661 individuals were included in the study group who had received yearly specific health checks in 2012. Even with the costly management and treatment, healthcare costs are manageable.

Hong Kong has a GDP of $51,168, with a reported cost of $52,307 per patient per year for hemodialysis and $27,529 for peritoneal dialysis. Dialysis cost and disease management costs are within affordability due to higher GDP.

Korea has a GPD of $33,147 per capita and ranks 4th in high-middle-income countries among the included studies in this review. Kim et al. [26] assessed the cost of CKD management at various stages. The initial burden was greatest owing to diagnosis and dialysis during the maintenance phase. the costs were partitioned as follows: direct medical-hospital costs (75.5% for HD, 84.0% for PD). The highest transport cost is reported from Korea at $1711 [26]. [29]. Korea has a well-developed public transportation system, including trains, subways, and buses. While this can help alleviate some transportation costs for individuals, the costs associated with maintaining and expanding public transportation infrastructure can contribute to higher overall transportation costs. They discovered that the cost was higher during the diagnosis phase than during the maintenance period. This is consistent with existing research. According to this study, the severity of the illness increases the cost of hospitalization. This is consistent with the findings of al-Awsat Tiwari et al. [37] from India, who discovered that days of hospitalization did not vary significantly with the severity of CKD but that the expense of hospitalization did. This cost can be reduced by reducing the frequency of hospitalizations and controlling disease progression.

Taiwan has a GDP of $32,339. In 2012, Taiwan's total healthcare expenditure per person was 15.3%. After accounting for a 3% discount rate, the total estimated lifetime health and well-being cost is significantly lower than that of industrialized nations. The total direct cost reported for hemodialysis was $23,479 and the direct cost reported for peritoneal dialysis was $19,300. We would anticipate that the difference in lifetime healthcare expenses between PD and HD would be smaller because the average cost associated with PD is typically lower than that of HD in many high-income nations. In this study; a broad perspective was adopted, we just extracted patient perspective direct medical costs as reported in the study, i.e. only those expenditures that directly affect patients like dialysis procedure cost per session, by excluding indirect costs and other societal perspective costs like caregiving costs, etc.

China has the 5th ranking for GDP of $14,096 of included studies from Asian countries. Hemodialysis is a significant cost driver [27] in China after Korea [26] and Taiwan [35] among Asian countries. The demand for dialysis services in China has outpaced the supply of dialysis centers and equipment. This limited availability can result in higher costs, as patients may need to travel long distances or face longer waiting times for treatment. The dialysis industry in Taiwan [35] and Korea [26] operate within a market economy, and factors such as competition, profit margins, and pricing strategies can influence the cost of dialysis services. The Yunnan Provincial Department of Human Resources and Social Security in China provided the statistics. In Yunnan province, the average annual social wage was $9543.8. As a result, the financial burden of ESRD patients was significantly more than the per capita income in Yunnan, a region with a complex topography and mountains. It is among China's poorest provinces. Patients find it inconvenient to constantly commute from the hospital to their homes, particularly in rural areas. to receive more extensive advantages [28]. Ma yu et al. study reported an annual per-patient cost for only hemodialysis of $11,967. Two studies from China, Ma yu et al., and Hong et al. have broad perspectives i.e., both societal and patient perspectives, only direct medical cost from the patient perspective was extracted, by excluding all indirect costs as reported in the study. Hong et al. reported the direct cost of different dialysis modules like hemodialysis as $24,988, APD $21,803, CAPD $15,218, and transplantation direct cost was reported as $24,191.

Jordan, with a GDP of $4851. The average management cost was $67. The AVF creation cost was reported to be only $181 in Jordan [13]. Lebanon, with a GDP of $4003, has the highest projected hospitalization expenditures. The mean annual expenditure for HD patients is 43.7% more than the gross domestic product per capita. The second-largest expense (13.67%) was related to medications. The most expensive drugs were Sevelamer, IV Iron, and EPO. Hospitalization was the third-highest expense.

The costs associated with patients, caregivers, and other components (such as transportation) contributed just a minor portion of the total expenses (4.18% and 4.09%, respectively). These elements collectively identify HD as a significant financial drain on the nation's healthcare system. Peritoneal dialysis cost reported is more than hemodialysis. The main cost drivers for HD were doctors, nurses, and treatment fees. For PD main cost drivers are the particular procedures or techniques that were employed.

Indonesia has a GDP of $4691, the hemodialysis cost reported from Indonesia was $6249 and the peritoneal dialysis cost is $3053. Due to their need for frequent hospital visits, HD households incurred higher transportation expenditures than PD households. Although patients in rural areas would need to spend several hours traveling to the clinic, the current study focused on urban settings where the average travel time from a patient's home to the hospital was less than an hour. Given the vast geographic heterogeneity in Indonesia, the budget effect analysis showed that the payer bears a smaller financial burden under the PD-first policy than under HD first. If PD was implemented, the payer may save a significant amount of money, considering that the present coverage rate is only 53% and that all patients will have access to dialysis by 2019.

Vietnam has a GDP of $4112, The average mean cost of lab investigations was $420, which was the same as mentioned for Lebanon [36] and Jordan [13], but much less in Vietnam [29]. The annual physician visit cost reported in Vietnam was much lower than that reported in Lebanon. The lower prices of lab tests and hospitalization in Vietnam compared to some other countries can be attributed to several factors, like Vietnam's lower cost of living and lower wages compared to many developed countries. This translates to lower Laboure costs for healthcare providers, which can contribute to lower overall healthcare costs, including lab tests and hospitalization. The healthcare market in Vietnam is relatively competitive, with numerous private and public healthcare providers. This competition can drive down prices as providers strive to attract patients by offering competitive pricing.

The average mean cost of transplantation was $55,795, which is much higher than reported in Iran has a GDP of $4234, and is lower than reported in Korea. Organ transplantation requires a sufficient supply of organs for the procedures to take place. In Iran, the demand for organs often exceeds the available supply, leading to higher costs as individuals may resort to alternative means to obtain organs, such as organ trafficking or traveling abroad for transplantation. The legal framework and regulations surrounding organ transplantation can impact the costs involved. In Iran [40] the sale of organs is prohibited, but the government has implemented a regulated system known as the Organ Transplantation Act, which allows living organ donation under certain conditions. The costs associated with complying with these regulations, such as medical evaluations, documentation, and monitoring, can contribute to higher transplantation costs.

India has a GDP of $2650, a reported direct cost of dialysis at $5490, hospitalization at $581, transportation at $273, and a total direct cost of RRT per patient per year reported was $6344, and for NRRT $1500. Josephine et al. reported the annual per-patient direct medical cost of only hemodialysis at $ 6987. The cost of hospitalization includes medication, nourishment, personnel fees, and bed charges. Variations in any of the above parameters affect hospitalization costs. Hospitalization costs were slightly higher in India than in China, even though both countries have the greatest prevalence of CKD. The transplantation surgical procedure cost reported from India was $1943. The total direct cost of annual per-patient expenditures for pre and post-care of transplantation was reported at $10,939 [43].

Medication costs are another significant component of direct costs. The average cost was $1248. This average cost was almost in line with Lebanon and Jordan [13]. Vietnam [29] has a low cost as compared to the mean average cost. Patients who have three or more exacerbations per year spend three times as much on medication as those who have two or fewer exacerbations. The addition of antibiotics and other acute treatment medicines to manage problems causes a rise in drug costs during an exacerbation. Medication costs were higher for patients in tertiary care facilities than for patients in primary care facilities. Medication costs were identified as a primary contributor to direct costs. Lebanon [36] and Jordan [13] have lower Laboure and operational costs compared to many developed countries. This can translate to lower costs for dialysis services, as healthcare providers have lower expenses related to staffing and facility maintenance. Controlling the frequency of exacerbations can thus lower drug costs, which in turn can lower direct costs.

The average cost of disease management was $67. The AVF creation cost was reported to be only $181 in Jordan [13]. Transportation costs were reported in five studies. The highest transport cost is reported from Korea at $1711 [26], and the lowest transport cost is reported from Vietnam at $24 [29]. Peritoneal dialysis was reported to be cost-effective in many studies. The average mean cost of dialysis was $69,755, which was around about as reported from Korea [26], and Taiwan [35], which has an almost distinct difference from the mean average cost and is very low as reported by Vietnam [29], Lebanon [36], and Jordan [13]. Dialysis centers require a skilled workforce, including nephrologists, nurses, and technicians. The costs associated with hiring and retaining qualified staff can contribute to higher dialysis costs. Lebanon [36] and Jordan [13] have lower Laboure and operational costs compared to many developed countries. This can translate to lower costs for dialysis services, as healthcare providers have lower expenses related to staffing and facility maintenance.

The disease contributes to a significant healthcare burden, as it requires ongoing medical management and specialized care [47, 48]. This places a strain on healthcare resources, including hospitals, clinics, and healthcare professionals [22, 49]. Furthermore, CKD can result in increased absenteeism and decreased productivity in the workforce, impacting economic productivity and potentially leading to increased healthcare costs. Understanding and addressing the direct burden of CKD is crucial for developing effective interventions and support systems for individuals with the disease. By mitigating the financial, physical, emotional, and societal impacts of CKD, it is possible to improve the overall well-being and outcomes of affected individuals and their communities.

Strength

A comprehensive summary of existing research on a specific topic allows for a broader understanding of CKD and its associated factors causing direct economic burden and comparison with each country's financial status. A systematic search strategy and inclusion criteria, help reduce selection bias and ensure a more objective assessment of the evidence. By pooling data from multiple studies, a systematic review can increase the statistical power and precision of the findings, allowing for more robust conclusions. In the existing literature, some areas are highlighted where further research is needed to enhance our understanding of the management of CKD.

Limitations

To provide the best possible information for clinical practice and policy, there are still significant gaps in the quantification of the direct costs revealed by patients with moderate- to late-stage chronic kidney disease. First, payers and, occasionally, employers are the main voices when it comes to reporting economic strain. Assessments of patients' out-of-pocket medical expenses between the insured and the uninsured are few. Secondly, there is a notable absence of data regarding the direct non-medical expenses linked to kidney disease before kidney failure. Even so, one of the most important aspects of the thorough evaluation of the financial burden of CKD is health care expenses. Systematic reviews often include studies published in a specific language or those available in specific databases. This can introduce language and publication bias, as studies published in other languages or non-indexed journals may be missed.

Conclusion

The direct costs associated with managing CKD exhibit significant variation across different countries, with higher costs observed in Asia. Key factors driving these costs were identified as dialysis, hospitalization, and medication. The severity of the disease strongly influenced the medication and hospitalization costs. By focusing on early-stage disease management and prevention of complications, it is possible to reduce the overall cost of managing CKD. This highlights the importance of optimizing CKD management strategies to minimize complications and control the progression of the disease in its initial stages. Dialysis, especially hemodialysis, is the main cost driver in the later stages of CKD. Peritoneal dialysis is cost-effective as compared to hemodialysis, as reported in many studies. Dialysis accounts for 60–80% of the total direct economic burden. While the economic burden of CKD has been extensively studied, there are still some research gaps that warrant further investigation. Some potential research gaps in the topic of the economic burden of CKD include the cost-effectiveness of interventions, novel payment models, policy implications, long-term cost, and outcomes. There is a need for more research evaluating the cost-effectiveness of different interventions for CKD, such as dialysis modalities (hemodialysis vs. peritoneal dialysis) and kidney transplantation. More simulation research studies must be conducted to estimate the cost-saving results from different interventions especially preventing the patient from being dependent on RRT by controlling disease progression. This approach could provide compelling evidence supporting investments in public health interventions targeting CKD prevention. Understanding the economic implications of these interventions can help in the guidance of treatment decisions and resource allocation.

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Author contributions
MN, ZT, SA, AJ, MFR, HK, SKT and AUR made substantial contribution by realization and designing the study. MN and AUR contribute substantially to the analysis and interpretation of data. All authors drafted the work or reviewed it critically for significant intellectual content. All authors reviewed, analyzed and approved the final version submitted for publication.

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Declarations

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